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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/788,410	03/01/2004	Robert L. Martuza	066683-0198	4953

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1632	

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10/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/788,410	MARTUZA ET AL.	
	Examiner	Art Unit	
	Wu-Cheng Winston Shen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-21 and 25-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-21 and 25-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03/01/2004* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response received on 08/06/07 has been entered. Claims 1-15 and 22-24 are cancelled. Claims 16-21 and 25-29 are pending. Claims 16-18, and 25-27 have been amended

Claims 16-21 and 25-29 are currently under examination.

This application is a DIV of 09/625,509, filed on 07/25/2000, now PAT 6,699,468, which is a DIV of 09/004,511, filed on 01/08/1998, now PAT 6,139,834, which is a **CON** of 08/478,800, filed on 06/07/1995 ABN, which is a **CON** of 08/264,581, filed on 06/23/1994, now PAT 5,585,096 (changes are in bold for emphasis).

The series of parent applications of instant application listed above is based on the Application Data Sheet filed on 08/06/2007.

Priority

1. As documented on the second Non-Final office action dated 04/11/2007, in the response to Non-Final rejection mailed on 10/03/2006, Applicant pointed out that the Examiner at the time omitted priority claim to U.S. Patent Application No. 08/264,581 (now Patent No. 5,585,096), filed June 23, 1994. The current Examiner acknowledges that the information regarding omitted priority to U.S. Patent Application No. 08/264,581 (now Patent No. 5,585,096) was indeed submitted by applicants as amendments of Specification filed on 9/7/2004. It is noted that the specification of U.S. Patent Application No. 08/264,581 (now Patent No. 5,585,096), filed June 23, 1994 supports the claims of instant application (See 4th paragraph, column 4, and 4th paragraph, column 5, U.S. Patent No. 5,585,096). Therefore, the priority of claims of instant application is determined to be 06/23/1994.

Claim Objections

2. Previous objection of claims 22-24 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, is ***withdrawn*** because claims 22-24 have been cancelled.

It is noted that claims 25-27 (lower numbers) are dependent from claim 28 (higher number). Appropriate correction (i.e. renumber the claims) is advised.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

3. Previous rejection of claims 16-21 and 25-29 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention since claim 16 recites the limitation "an alteration, *relative to wild type*, in γ34.5 gene" fails to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is ***withdrawn*** because the claims have been amended deleting the phrase "relative to wild type".

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 16-18 and 29 remain rejected under 35 U.S.C. 102(b) as being anticipated by Chou et al. (Chou et al., Mapping of herpes simplex virus-1 neurovirulence to $\gamma_1$34.5, a gene nonessential for growth in culture. *Science* 250(4985): 1262-6, 1990). Applicant's arguments filed 08/06/2007 have been fully considered and they are not persuasive. Previous rejection is ***maintained*** for the reasons of record advanced on pages 5-6 of the office action mailed on 04/11/2007.

For clarity and completeness of this office action, the rejection documented on pages 5-6 of the office action mailed on 04/11/2007 is reiterated below, with editions deleting part of the rejection relevant to claim 22-24 as a result of cancellation of these claims. It is noted that $\gamma_1$34.5 gene, which encodes ICP34.5 protein, disclosed by prior art Chou et al., is the same gene named γ34.5 as disclosed in the instant application.

Chou et al. teach that four recombinant HSV-1 viruses (Herpes Simplex Virus 1) were genetically engineered to test the function of the $\gamma_1$34.5 gene. These were (i) a virus from which *both copies of the gene were deleted*, which is encompassed by claim 17 of instant application, (ii) a virus containing a stop codon in both copies of the gene --- which is encompassed by claim 18 of instant application, (iii) a virus containing after the first codon an insert encoding *a 16-amino acid epitope known to react with a specific monoclonal antibody,* which is encompassed by claim 16 of instant application, and (iv) a virus in which the deleted sequences were restored.

With regard to claim 29 of instant application, a pharmaceutically acceptable vehicle reads on water, which is encompassed by the teachings of Chou et al.

Thus, Chou et al. clearly anticipates claims 16-18 and 29 of instant invention.

Applicant's arguments

With regard to whether Chou et al. anticipate Claims 16-18 and 29 of instant application, Applicant argues that Chou et al. disclose an HSV with mutated γ34.5 gene that contains an insert of a 16-amino acid epitope, which does not meet the recitation of claim 16, an "expressible non-herpes simplex virus nucleotide sequence encoding a desired protein". Specifically, Applicant argues that Chou makes reference to another publication by Hubenthal-Voss et al., J. of Virology 62:454-62 (1988), which describes the peptide epitope in question. (See Chou at page 1264, right column, lines 27-32). Applicant elaborates that Hubenthal-Voss stating that a 15-amino acid peptide comprises the sequence of the N-terminal domain of ICP4 (page 456, right column, lines 6-9), which is a herpes simplex virus protein. In the C- terminus, Chou's peptide is one amino acid longer than Hubenthal-Voss', due to the introduction of a restriction endonuclease site during cloning. Applicant argues that, nevertheless, one skilled in the art would have appreciated that Chou's peptide comprises the sequence of the HSV protein, ICP4. By contrast, the claimed invention relates to a herpes simplex virus with a genome that comprises an expressible ***non-herpes simplex virus*** nucleotide sequence encoding a desired protein and an alteration in the γ34.5 gene. Moreover, Applicant argues that Chou's virus with the 16-amino acid insert is "moderately virulent" (See abstract, lines 10-11), while the virus of Applicants' invention, by virtue of the recited "alteration in the γ34.5 gene," is "not neuro-virulent." See specification at page 1, line 8. Thus, Applicant concludes that the prior-art HSV does not embody each and every aspect of the presently claim invention.

Response to Applicant's arguments

Applicant's arguments filed on 08/06/2007 have been fully considered and they are not persuasive. First, Applicant indicates in the response filed on 08/06/2007 that Hubenthal-Voss et al. 1988 cited by Chou et al. has been appended as Exhibit A. However, the Examiner cannot find Exhibit A available of the record. To facilitate the prosecution of instant case, the Examiner has listed Hubenthal-Voss et al. in the PTO-892 form (Hubenthal-Voss et al., Mapping of functional and antigenic domains of the alpha 4 protein of herpes simplex virus 1. *J Virol.* 62(2): 454-62, 1988). Second, the limitation "an expressible non-herpes simplex virus nucleotide sequence encoding a desired protein" recited in claim 16 clearly reads on the tagged version of γ34.5 gene with insertion after first codon introducing part of the coding sequences of ICP4 of HSV for the reasons as follows: (i) the tagged version of γ34.5 gene taught by Chou et al. encodes a fusion protein with additional 16 amino acid residues inserted at N-terminus, which meets the requirement "nucleotide sequence encoding a desired protein", and (ii) introduction of one more codon, resulting from addition of a restriction enzyme site, that was not in the HSV genome reads on *non-herpes simplex virus* nucleotide sequence, because this nucleotide sequence is not normally present in HSV. Third, the Examiner's interpretation is that the nucleotide sequences encoding the epitope, originated from part of the coding sequences of ICP4, being moved out of its genomic content as the ICP4 gene, are no longer considered as herpes simplex virus nucleotide sequence *per se* because the definition of HSV or non-HSVgene (or nucleotide sequences) should be defined within the context of the gene under consideration. Furthermore, an extrapolation from Applicant's arguments that nucleotide sequences of gene ICP4 being engineered as part of γ34.5 gene in HSV genome, and the added nucleotide

sequences of ICP4 gene *in the context of γ34.5 gene* are still considered as HSV sequences, will lead to the conclusion that there is no such a distinction between the terms "endogenous" versus "exogenous" genes as conventionally accepted genetic terminology because, based on Applicant's arguments, all genes are composed of the four different nucleotides (A, T, G, C) and these nucleotides can be moved freely out of any specific context of a given gene and be considered as endogenous.

Applicant's arguments regarding Chou's virus being "moderately virulent" and the virus claimed in instant application being "not neuro-virulent", are found not persuasive because (i) virulence of the virus is not recited in the claims and, (ii) even if virulence were recited in the claims, it is considered as an inherent characteristics associated with structures of the virus, not pertaining to the structures of the virus itself.

Therefore, Chou et al. clearly anticipates claims 16-18 and 29 of instant invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (c) or 1.321 (d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Previous provisional rejection of claims 16-29 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7-18 of copending Application No. 10/748,233 is ***maintained*** for the reasons of the record. Although the conflicting claims are not identical, they are not patentably distinct from each other because both are directed to the same herpes virus construct. In each case the claims as a whole set forth a herpes virus comprising an alteration in γ34.5, a heterologous gene of interest and an alteration in the ribonucleotide reductase gene. For example claim 20 of instant application and claim 10 of copending Application No. 11/748,233 both set forth that the HSV is G207.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Previous provisional rejection of claims 16-29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 35-39, 43-46 of copending Application No. 11/097,391 is ***maintained*** for the reasons of the record. Although the conflicting claims are not identical, they are not patentably distinct from each other because

both are directed to the same herpes virus construct. In each case the claims as a whole set forth a herpes virus comprising an alteration in γ34.5, a heterologous gene of interest and an alteration in the ribonucleotide reductase gene. For example claim 20 of instant application and claim 39 of copending Application No. 11/097,391 both set forth that the HSV is G207.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments

Applicant states that because these rejections are provisional, Applicants choose to defer any action until an actual double-patenting rejection is made, or until there is indication of allowable claims in the present application.

Response to Applicant's arguments

The provisional obviousness-type double patenting rejections listed above are maintained of the records, as Applicant does not wish to address the rejection at this stage of prosecution.

Conclusion

6. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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